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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/985,689	11/05/2001	Yuji Hatada	215483US0	4010

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EXAMINER	
SWOPE, SHERIDAN	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/12/2003 15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/985,689	HATADA ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *3-9,11-14 and 16-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,10 and 15* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7, 12.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election, with traverse, of Invention I, drawn to alkaline proteases, and Species D, a variant of SEQ ID No: 1 wherein position 369 has been altered, in Paper No. 14 is acknowledged. The reasons for restriction are described in Paper No. 13. Traversal is based on the following arguments by the Applicant.

(1) "In regards to Groups I and II, the Office has characterized the relationship between these groups as product and process of making and product and process of use". Citing MPEP 806.05(h), the Office concludes that the product as claimed 'can be made by another and materially different process, such as by synthetic peptide synthesis or purification from the natural source'. Applicants note that the Office has merely stated an unsupported conclusion. The Office has failed to show that the alleged processes "synthetic peptide synthesis or purification from the natural source' is materially different from the claimed process." This argument is not found to be persuasive. It is unclear to the Office what is meant by this argument. Groups I and II have not been characterized by the Office as product and process of making and product and process of use.

The proteins of Group I and the nucleic acids of Group II were characterized as distinct products. As previously stated inventions in this type of relationship are patentably distinct when if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Although the DNA molecule and protein are related, since the DNA encodes the specifically claimed protein, they are distinct inventions because they are physically and functionally distinct chemical entities and, furthermore, the protein product can be made by

another and materially different process, such as by synthetic peptide synthesis or purification from the natural source. In addition, the DNA may be used for processes other than the production of the protein, such as nucleic acid hybridization assay. That synthetic peptide synthesis and purification of a protein from the natural source are materially different processes from recombinant production of a protein is common knowledge in the art. Synthetic peptide synthesis comprises in vitro reactions wherein, amino acids are chemically linked to a growing polypeptide chain. Purification of a protein from its natural source comprises harvesting appropriate cells or tissues, homogenization, and fractionation by a series of steps that can include precipitation, centrifugation, ion exchange chromatography, hydrophobic chromatography, size exclusion, chromatography, and/or affinity chromatography. In contrast, recombinant production of a protein comprises isolation of a polynucleotide encoding the desired protein, subcloning of said polynucleotide into an appropriate expression vector, transformation or transfection of the polynucleotide-containing expression vector into a host cell, and allowing the host cell to express the encoded protein. Since each of these methods of producing the recited protein do not recite the same reagents or steps, the conditions required, for concluding that the nucleic acid and encoded protein are distinct inventions, are met.

(2) "The Office further states that 'the DNA may be used for processes other than the production of the protein, such as nucleic acid hybridization assay.' Applicants note that the Office has merely stated an unsupported conclusion and has failed to show that the alleged process 'nucleic acid hybridization assay' is materially different from the claimed process." This argument is not found to be persuasive. It is common knowledge in the art that, production of a recombinant protein and hybridization analysis are different methods. The steps for recombinant

production of a protein are described in the prior paragraph. Nucleic acid hybridization comprises resolving the DNA or RNA for analysis by SDS-PAGE, transferring the resolved nucleic acid molecules to a solid support, such as a nitrocellulose membrane, then blocking the membrane with an appropriate buffer, incubating the membrane with the recited nucleic acid molecule used as a "probe", washing away the unbound probe, and detecting the binding of the probe to one or more nucleic acid molecules on the solid support. Since the methods of using the nucleic acid molecule for recombinant production of the encoded protein and hybridization analysis do not recite the same reagents, steps, or outcome, the conditions required for concluding that the nucleic acid and encoded protein are distinct inventions, are further supported.

(3) "Applicants note that Groups I-II are classified in the same class, 435, and respectfully submit that a search of all the claims would not impose a serious burden on the Office". This argument is not found to be persuasive. There are many subclasses in each class. Groups I and II are classified class 435, subclass 212, and class 435, subclass 252.33, respectively. Since Groups I and II have different classification, a search for one group would not encompass a search for the other group and searching all groups would represent a burden on the Office.

(4) "The Office has not provided any reasons or examples to support a conclusion that the species are indeed patentably distinct." As stated by 35 U.S.C. 101, "Whoever invents or discovers any new …composition of matter … may obtain a (emphasis added by Examiner) patent therefore". Each species represent a structurally different polypeptide. Therefore, where

structural identity is required, such as for generation of antibodies and in pharmaceutical compositions, the different polypeptides have different effects.

For these reasons and those described in Paper No. 13, the restriction requirement is still deemed proper and is therefore made FINAL.

Claims 3-9, 11-14, and 16-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Inventions, there being no allowable generic or linking claim. Claims 1, 2, 10, and 15, drawn to alkaline proteases wherein position 369 of SEQ ID No: 1 has been altered, are hereby examined.

Specification-Objections

35 U.S.C. 112, first paragraph, requires the specification to be written in "full, clear, concise, and exact terms." The specification is replete with terms, which are not clear, concise and exact. The specification should be revised carefully in order to comply with 35 U.S.C. 112, first paragraph. Examples of some unclear, inexact or verbose terms used in the specification are listed below. A new specification in proper idiomatic English should be submitted.

The abstract is comprised of a single run-on sentence. Also, it is not clear whether "an enzyme" on line two is referring to the alkaline protease recited on line one. "Detergency" is not found in either, the Random House College Dictionary, Steadman's Medical Dictionary, or the Oxford Dictionary of Biochemistry and Molecular Biology.

Page 1, line 17: It is not clear what is meant by "market scale".

Page 5 line 19-page 7 line 6: These pages constitute a single run-on sentence which lack clarity. For example, the statement "in the alkaline protease of the present invention, an amino acid residue at (a) position 84 … of SEQ ID NO: 1 or at a position corresponding thereto has

been deleted or selected from: at position (a): an arginine residue. It is not clear what the phrase "selected from an arginine residue" means. See below under 35 U.S.C. 112, second paragraph, for further description of the problem.

Page 17 line 15-16: "...under the treating conditions at 40°C ..." is not proper idiomatic English.

Figure Legends

The figure legends are objected to because they lack clarity and do not state which wild-type and variants are used.

Claims-Objections

Claim 1 is objected to for not having a period (.) at the end.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Double Patenting

It is noted that copending Application SN# 10/385,662 has the same title and some of the same inventors of the instant application suggesting that, the claims of 10/385,662 and this application may recite the same or overlapping inventions. Since 10/385,662 is not presently available for review, no determination has been made as to whether or not a double patenting rejection over the claims from 10/385,662 should be applied to the claims of the instant application. If, upon availability of the above application to the Examiner, it is determined that there are conflicting claims between 10/385,662 and the instant application, double patenting will not be considered as new ground(s) of rejection.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 10, and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Recitation in Claims 1 and 2 of "An alkaline protease, ...wherein an amino acid residue at ... position 369 of SEQ ID NO: 1... has been deleted or selected from ...an apartic acid residue" is unclear. It is not clear what the phrase "selected from an aspartic acid residue" means. Two possible meanings are: (1) wherein the residue at 369 of SEQ ID NO: 1 is an aspartic acid or (2) wherein the aspartic acid residue at 369 of SEQ ID NO: 1 is mutated. Clarification is required. For purposes of examination, it is assumed that the meaning of "selected from an aspartic acid residue" is: wherein the residue at 369 of SEQ ID NO: 1 is an aspartic acid. Claims 10 and 15, being dependent from Claims 1 and 2, are rejected for the same reasons.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 10, and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the alkaline protease of SEQ ID NO: 1, does not reasonably provide enablement for any alkaline protease wherein the residue corresponding to

369 in SEQ ID NO: 1 is an aspartic acid or any alkaline protease having at least 60% homology to SEQ ID NO: 1, wherein the residue corresponding to 369 is an aspartic acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claim 1 is so broad as to encompass any polypeptide with alkaline protease activity wherein the position corresponding to 369 of SEQ ID NO: 1 is an aspartic acid. Claim 2 is so broad as to encompass any polypeptide with alkaline protease activity and having at least 60% identity with SEQ ID NO 1 wherein the position corresponding to 369 is an aspartic acid. The scope of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired alkaline protease activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of SEQ ID NO: 1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable. In addition, one skilled in the art

would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of Claim 1, which is so broad as to encompass any polypeptide with alkaline protease activity wherein the position corresponding to 369 is an aspartic acid. The specification does not support the broad scope of Claim 2 which, encompasses all polynucleotide sequences that encode a protein having alkaline protease activity and having at least 60% identity with SEQ ID NO: 1, wherein the position corresponding to 369 is an aspartic acid. The specification does not support the broad scope of Claims 1 and 2 because the specification does not establish: (A) all alkaline proteases having an aspartic acid at the position corresponding to 369; (B) regions of any alkaline protease protein structure which may be modified without effecting the activity of said alkaline protease; (C) the general tolerance of the activity of any alkaline protease to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices of protein sequences is likely to be successful.

Since Claims 10 and 15 further recite detergent compositions comprising the alkaline proteases of Claims 1 and 2, Claims 10 and 15 are also rejected under 35 U.S.C. 112 first paragraph due to lack of enablement for the same reasons discussed above.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any alkaline protease wherein the position corresponding to 369 of SEQ ID NO: 1 is an aspartic acid and having an enormous number of amino acid

modifications or any alkaline protease wherein the position corresponding to 369 is an aspartic acid and having an enormous number of amino acid modifications of the alkaline protease of SEQ ID NO: 1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1, 2, 10, and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 10 are directed to a genus of polypeptides having alkaline protease activity wherein the position corresponding to 369 in SEQ ID NO: 1 is an aspartic acid residue. Claims 2 and 15 are directed to a genus of polypeptides having alkaline protease activity wherein the protease has at least 60% identity with SEQ ID NO: 1 and the position corresponding to 369 is an aspartic acid residue. The specification teaches the structure of only a single representative species of such polypeptides, SEQ ID NO: 1. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding an alkaline protease. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the

claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 10, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Hitomi et al, 1999, Tobe et al, 1997, or Christianson et al, 1998. Hitomi et al teach an alkaline protease that is 100% identical to SEQ ID NO: 1, wherein residue 369 is an aspartic acid. Tobe et al teach a polynucleotide that encodes an alkaline protease having 88% identity with SEQ ID NO: 1, wherein the residue corresponding to 369 of SEQ ID NO: 1 is an aspartic acid. Christianson et al teach a polynucleotide that encodes a protease having 94% identity with SEQ ID NO: 1, wherein the residue corresponding to 369 of SEQ ID NO: 1 is an aspartic acid. Each of Hitomi et al, Tobe et al, and Christianson et al further teach that their protease can be used in a detergent composition. Therefore, Claims 1, 2, 10, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Hitomi et al, 1999, Tobe et al, 1997, or Christianson et al, 1998.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 703-305-1696. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone

numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sheridan L. Swope, Ph.D.

REBECCA E. PROUTY
PRIMARY EXAMINER
1600